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Application :	09587111	**Examiner :**	Ulm	**GAU :**	1646
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DOC CODE	DOC DATE	MISCELLANEOUS
☐ 1449		☑ Continuing Data
☐ IDS		☐ Foreign Priority
☐ CLM		☐ Document Legibility
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☐ SRFW		☐ Other
☐ DRW		
☐ OATH		
☐ 312		
☐ SPEC		

[RUSH] **MESSAGE:**

- First line of continuing data on Palm sheet is not in specification.
- "CIP" is cited for 2nd and 3rd lines on bib sheet, but only claims priority is stated in specification.

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[XRUSH] **RESPONSE:**

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REV 10/04

NOVEL MEMBERS OF THE CAPSAICIN/VANILLOID RECEPTOR FAMILY OF PROTEINS AND USES THEREOF

Related Applications

This application claims priority to U.S. provisional Application No. 60/108,322, filed on November 13, 1998, U.S. provisional Application No. 60/114,078 filed on December 28, 1998, U.S. Patent Application Serial No.: 09/258,633 filed on February 26, 1999, and U.S. Patent Application Serial No.: 09/421,134 filed on October 19, 1999, incorporated herein in their entirety by this reference.

Background of the Invention

Pain is initiated when the peripheral terminals of a subgroup of sensory neurons are activated by noxious chemical, mechanical or thermal stimuli. These neurons, called nociceptors, transmit information regarding tissue damage to pain-processing centres in the spinal chord and brain (Fields, H.L. *Pain*, McGraw-Hill, New York, 1987). Nociceptors are characterized in part, by their sensitivity to capsaicin, a vanilloid-containing compound, and a natural product of capsicum peppers that is the active ingredient of many "hot" and spicy foods. In mammals, exposure of nociceptor terminals to capsaicin leads initially to excitation of the neuron and the consequent perception of pain and local release of inflammatory mediators. With prolonged exposure, nociceptor terminals become insensitive to capsaicin, as well as to other noxious stimuli (Szolcsanyi, J. in *Capsaicin in the Study of Pain* (ed. Wood, J.) 1-26 (Academic, London, 1993). This latter phenomenon of nociceptor desensitization underlies the seemingly paradoxical use of capsaicin as an analgesic agent in the treatment of painful disorders ranging from viral and diabetic neuropathies to rheumatoid arthritis (Campbell, E. in *Capsaicin and the Studyof Pain* (ed. Wood, J.) 255-272 (Academic, London, 1993); Szallasi, A. *et al.* (1996) *Pain* 68, 195-208). Some of this decreased sensitivity to noxious stimuli may result from reversible changes in the nociceptor, but the long-term loss of responsiveness can be explained by death of the nociceptor or destruction of its peripheral terminals following exposure to capsaicin (Jancso, G. *et al.* (1977) *Nature* 270, 741-743).

The cellular specificity of capsaicin action and its ability to evoke the sensation of burning pain have led to speculation that the target of capsaicin action plays an important physiological role in the detection of painful stimuli. Indeed, capsaicin may elicit the perception of pain by mimicking the actions of a physiological stimulus or an endogenous ligand produced during tissue injury (James, I.F., Kinkina, N.N. & Wood, J.N. in *Capsaicin in the Study of Pain* (ed. Wood, J.N.) 83-104 (Academic, London, 1993).

Caterina M.J. *et al.* have recently determined the molecular basis underlying this phenomenon by characterizing a functional cDNA that encodes a vanilloid receptor (VR-1) in rat

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Bib Data Sheet

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09/587,111	06/02/2000 RULE _	435	1643	MNI-062CP2DV1

APPLICANTS

Rory A.J. Curtis, Southborough, MA ;

**** CONTINUING DATA ***************************

THIS APPLICATION IS A DIV OF 09/439,165 11/12/1999
WHICH IS A CIP OF 09/421,134 10/19/1999 ABN
AND CLAIMS BENEFIT OF 60/108,322 11/13/1998
AND CLAIMS BENEFIT OF 60/114,078 12/28/1998

**** FOREIGN APPLICATIONS *********************

IF REQUIRED, FOREIGN FILING LICENSE GRANTED ** 07/27/2000

Foreign Priority claimed	STATE OR COUNTRY	SHEETS DRAWING	TOTAL CLAIMS	INDEPENDENT CLAIMS
☐ yes ☐ no	MA	35	50	6
35 USC 119 (a-d) conditions met ☐ yes ☐ no ☐ Met after Allowance				
Verified and Acknowledged Examiner's Signature Initials				

ADDRESS

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TITLE

Novel members of the capsaicin/vanilloid receptor family of proteins and uses thereof

FILING FEE RECEIVED	FEES: Authority has been given in Paper	
1724	No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit